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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,982	10/09/1998	FREDERIC KLEIN	032475-001	9420

21839 7590 10/11/2002

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	19

DATE MAILED: 10/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/155,982	Klein
Examiner	**Art Unit**
Portner	1645

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 22, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-39* is/are pending in the application.

4a) Of the above, claim(s) *20-21,23,25,27, 30(protein),32,36,38-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-19, 22, 24, 26,28-30(monoclonal antibody), 31, 33-35, 37* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *17-39* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 17-39 are pending.

Claims 20-21, 23,25,27, 30(protein), 32,36,38-39 are drawn to a non-elected invention.

Claims 17-18, 19, 22,24,26,28-29, 30 (monoclonal antibody kits), 31,33-35 and 37, have been amended and are under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

2. Newly submitted claim 30, 34 and 35 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The elected invention was directed to kits that comprise monoclonal antibodies. The newly amended claim 30 is directed to three different kits, specifically monoclonal antibody kits, protein kits, and anti-antibody kits. The kits directed to protein and anti-antibody kits are herein withdrawn as being directed to a non-elected invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 30, 34-35 those species not examined previously are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Objections/*Rejections Withdrawn*

3. The objection to the disclosure because of the noted informality at page 24, line 11, in light of the amendment to delete the blank space is defined by [ ].

4. Claim 24 rejected under 35 U.S.C. § 112, first paragraph as failing to provide an enabling disclosure, in light of the Deposit Declaration enabling a single species of hybridoma within the scope of the claim.

5. Claims17 (partially withdrawn)-19, 22, 24, 26-29,30,33-35 and 37 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the instantly claimed invention, in light of the amendment of claims 17 and 19 to recite specific species of bacteria to which the claimed monoclonal do not cross react.

6. Claims 17 and 30 (kit claims) rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production of monoclonal antibodies that specifically bind to T.equigenitalis and immunogenic compositions that comprise monoclonal antibodies, does not reasonably provide enablement for the use of any monoclonal antibody for prevention or treatment of infection and disease caused by T.equigenitalis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in **scope** with these claims, in light of the amendment of the claims to recite monoclonal antibodies for detecting an immunological reaction.

7. Claim 18, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of claim 18 to define the specific binding of one of 4 different Taylorella antigens.

8. Claim 26 rejected under 35 U.S.C. 112, second paragraph recites the phrase "which may contain T.equigenitalis, into contact with an effective quantity of at least one monoclonal antibody or a fragment thereof", in light of the amendment of the claim to recite --Fv, Fab or F(ab')2--.

9. Claim 30 rejected under 35 U.S.C. 112, second paragraph recites the phases "reagents, for carrying out the intended immunologic reaction," and "optionally, reagents for blocking the non-

antigen-antibody reactions.", in light of the amendment of claim (29 renumbered claim 30 under 37 CFR 1.126) to recite the term "detecting" which clarifies the invention.

Rejections Maintained

10. Claims 17 (partially maintained) and 31 (dependent upon claim 17), rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the instantly claimed invention, for reasons of record in paper number 7, paragraph 17; paper number 10, paragraph 16 (pages 6-7) and paper number 12, paragraph 16, with respect to prevention and treatment of infection using a single monoclonal or combination of monoclonals not shown to treat or prevent infection.

11. Claim 19 rejected under 35 U.S.C. 112, second paragraph recites the phrase "the required monoclonal antibodies", for reasons of record in paper number 12, paragraph 14.

12. Claims 17, 18, 19, 22, 24, 26, 28, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Akuzawa et al (1996) for reasons of record in paper number 7, paragraph 19 and Response to arguments, in paper number 10, paragraph 20. See attached English translation of the Japanese reference.

13. Claims 17,19, 26, 28 rejected under 35 U.S.C. 102(b) as being anticipated by Friedrich (1995), for reasons of record in paper number 7, paragraph "o", page 12, and response to arguments in paper number 10, paragraph 18.

14. Claim 18 rejected under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Sugimoto et al (1988), for reasons of record in paper number 7, paragraph 21 and Response to Arguments, in paper number 10, paragraphs 22 and 23.

15. Claim 18 under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Corbel et al (1982) for reasons of record in paper number 7, paragraph 22, and Response to Arguments, in paper number 10, paragraph 24.

16. Claims 17, 19, 22, 24, 26, 28-29, 31, 35 and 37 rejected under 35 U.S.C. 103(a) as being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow:Antibodies, A Laboratory Manual (1988,chapters 4,6,9, 14-15) for reasons of record in paper number 7, paragraph 23, and Response to Arguments, in paper number 10, paragraphs 26, and 27.

17. Claims 30, 33 and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Tainturier in view of Friedrich and Harlow further in view of Foster (US Pat. 4,444,879), for reasons of record in paper number 7, paragraph 24, and Response to Arguments, in paper number 10, paragraph 28.

Response to Arguments

18. Applicant's arguments filed July 22, 2002 have been fully considered but they are not persuasive.

19. The rejection of claims 17 and 31 ~~rejected~~ under 35 U.S.C. 112, first paragraph, (scope), as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the instantly claimed invention, is traversed on the grounds that the claimed monoclonal antibodies do not cross react with eigtht other specified bacteria, the monoclonal antibodies are taught to be formulated into a vaccine in Example 6, and could used.

20. It is the position of the examiner that the scope of enablement was directed to the recitation of "pharmecutical composition", wherein the composition encompasses the utilization of a single type monoclonal that specifically binds to Taylorella (claim 17), but is not a monoclonal antibody that binds to a single epitope that prevents infection and disease or has been shown to treat pre-existing infection. The monoclonals specifically bind to the antigens of T.equigenitalis, but are not defined to be opsonic antibodies. No single epitope has been described as being an epitope to which a monoclonal antibody of the invention binds that provides passive protective immunity. The rejection is maintained for reasons of record in paper number 7, paragraph 17, paper number 10, paragraph 16, pages 6-7 and paper number 12, paragraph 16 (claim 30 renumbered to be claim 31 under rule 37 CFR 1.126).

21. The rejection of claim 19 under 35 U.S.C. 112, second paragraph for reciting the phrase "the required monoclonal antibodies", is asserted to have been obviated through the deletion of the word "required".

22. It is the position of the examiner that the word "required" has not been deleted from the claims. Applicant's arguments are not commensurate in scope with the instantly pending claims.

23. The rejection of claims 17,19, 26, 28 under 35 U.S.C. 102(b) as being anticipated by Friedrich (1995), is traversed on the grounds that Applicant's only received one page of the

Friedrich article and this is believed to be in error; a complete translation is necessary to be proper.

24. It is the position of the examiner that the cited Friedrich (1995) reference is only a single page, specfically page 13. The citation reads "Pferdeheilkunde, 1995, Vol. 11, No1 (Jan-Feb), P13. Only page 13 is required and has been provided to Applicant in English (see col. 2). Column is in German and Column 2 is the translation of the German into English. The "Results" submitted by Applicant were not applied to the claims. The source of the "Results" are not the Pferdeheilkunde article applied to the claims. The pages from the "Results" are not numbered. Data in the figures is missing (Figures 1-8). The information was not presented in a Declaration under 37 CFR 1.132. The "Results" submitted appears to be a draft for a manuscript prior to publication, but the source and the authors of the manuscript have not been identified to be Friedrich, U.

Upon consideration of page 19 (counting from the first page of the submitted results), the examiner found the statement "In the study of potential cross-reactions of all the mAb used with representatives of different bacterial species, no antigenic affinities could be detected". Five pages from the end of the document the statement was made "[S]ince the mAb TF II8D4 and TF III 11B5 detect all the Taylorella strains under test with the ELISA technique, did not show any cross-reactions with previously tested bacterial species and these antibodies are able to react with the IFT technique, it is possible to establish a rapid test based on IFT".

The data presented in the "Results" section submitted, the reference source not being one applied to the claims, is not convincing. The rejection of the claims is maintained for reasons of record.

25. The rejection of claims 17-19, 22, 24, 26, 28, 31 under 35 U.S.C. 102(b) as being anticipated by Akuzawa et al (1996) is traversed on the grounds that the monoclonal antibody NA-1 did not react with antigens used in immunization, that NA-1 recognized polysaccharide or LPS components in the outer membrane and asserts that the LPS of T.equigenitalis has a molecular weight of 22 kDa.

26. It is the position of the examiner that the immunogen used for induction and production of monoclonal antibodies was "external cell membranes" of Taylorella, the selected monoclonal antibodies were not cross reactive with 9 strains of bacterial pathogens that cause equine uterine infection, to include Klebsiella and E.coli and the antigen with which the monoclonal NA-1 reacted presented an epitope that is heat resistant, and migrated to about 28-44 kDa, the epitope being a polysaccharide or lipopolysaccharide epitope.

Clearly the monoclonal antibody NA-1 of Akuzawa et al was non-cross reactive (see paragraph 2 of translated abstract), reactive with a heat resistant antigen (see paragraph 3, of translated abstract), did not react with protein antigens (see paragraph 3 of translated abstract), was determined to be a polysaccharide containing epitope based upon molecular analysis and the epitope presented itself in more than one relative molecule weight molecule, one of which was an

about 28 kDa molecule which reads on the immunoreactivity for a 22 kDa molecule. Relative molecular weights permit variation in the relative molecular weight, and the 28 kDa polysaccharide molecule of Akuzawa et al reads on the recited 22 kDa antigen of the claims.

There is no requirement for the claimed monoclonal antibodies to react with all strains of Taylorella equigenitalis. The claimed monoclonal antibodies are required not to cross react with other bacteria and the monoclonal antibodies of Akuzawa et al did not cross react with 9 other pathogens derived from horse uteruses. Clearly NA-1 reads on the recited monoclonal antibody that specfically binds to a 22 kDa polysaccharide containing antigen.

With respect to NA-2, the monoclonal antibody was selected based upon non-cross reactivity with other strains of bacteria derived from horse uteruses (see English translation paragraph 2). Clearly NA-2 anticipates the claims directed to a non-cross reactive monoclonal antibody that is immunoreactive with T.equigenitalis proteineous antigens (English translation paragraph 3). The rejection is maintained for reasons of record.

27. Claim 18 rejected under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Sugimoto et al (1988), is traversed on the grounds that a translation of Friedrich has not been provided, that the monoclonal antibodies of Friedrich have not been established to be specific to Taylorella based upon any evidence that is of record, and the size of the outer membrane antigens of Sugimoto fail to remedy the deficiences of Friedrich.

28. It is the position of the examiner that an English translation of the applied one page reference was provided to Applicant, that Applicant provided evidence that at least two of the monoclonal antibodies of Friedrich are non-cross reactive monoclonal antibodies (see discussion above), if in fact that the "Results" data presented is from Friedrich, relative to the applied document.

The combination of Friedrich (1995) in view of Sugimoto et al sets forth a prima facie case of obviousness based upon the clear teaching and suggestion of the prior art to develope a specific monoclonal antibody based diagnostic immunoassay for the purpose of better proof of diagnosis (Fredrich), wherein the monoclonal antibodies are not cross reactive with other pathogenic bacteria associated with a horse uterus (Akuzawa et al) and would recognize surface associated antigens that are diagnostic (proteins and polysaccharide containing antigens, Akuzawa et al). The rejection is maintained for reasons of record.

29. Claim 18 under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Corbel et al (1982) is traversed on the grounds that there is no translation of Friedrich, the antibodies of Friedrich are non-specific, and the LPS antigen of Corbel does not define a monoclonal antibody of claim 18.

30. It is the position of the examiner that a translation was provided, the antibodies of Friedrich (1993) were key to "allow a prompt diagnosis of CEM but also give a better proof" of diagnosis and Applicant provided evidence that Friedrich produced non-cross reactive monoclonal antibodies.

Clearly Friedrich taught the production of monoclonal antibodies to Taylorella equigenitalis antigens to have the advantage of a better proof and a prompt diagnosis of infection. Corbel et al characterized major specific Taylorella equigenitalis antigens (title), to include the polysaccharide surface antigens, shown to be immunogenic and immunoreactive. Eleven distinct immunoreactive antigens were disclosed (see page 533, last sentence) and the relative molecular weights provided in Table 1, page 534. Friedrich (1995) in view of Corbel et al (1982) set forth a prima facie case of obviousness because the person of ordinary skill would be motivated to produce monoclonal antibodies to the major antigens of Taylorella equigenitalis for prompt diagnosis of infection in horses associated with reproductive failure.

31. The rejection of claims 17, 19, 22, 24, 26, 28-29, 31, 35 and 37 under 35 U.S.C. 103(a) as being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow:Antibodies, A Laboratory Manual (1988,chapters 4,6,9, 14-15) is traversed on the grounds that Friedrich requires an English translation, that Tainturier does not show monoclonal antibodies to the antigens, that recognize a T.equigenitalis epitope and does not cross readt with the bacterium recited in claim 17.

32. It is the position of the examiner that a translation of Friedrich was provided, that Tainturier et al teach the generation of polyclonal antibodies that are non-cross reactive with other bacterial pathogens (see Table 3, top of page 359), and Friedrich and Harlow provide the motivation and reasonable expectation of success of obtaining non-cross reactive monoclonal antibodies that

provide an advantage over monoclonal antibodies, with respect to specificity, and prompt diagnosis of infection, as well as the teaching of Tainturier which shows antigens that are specific to T.equigenitalis (see Table 2, page 357). Ex parte Erlich 3 USPQ2d 1011 decision, case law was established for obviousness; specifically, it is obvious to make a monoclonal antibody to a known antigen for the purpose of attaining improved specificity of antibody binding.

Tainturier et al teach the importance of non-cross reactive antibodies, and specific antigens found only in T.equigenitalis; Friedrich teaches that monoclonal antibodies provide an advantage for a better proof and a prompt diagnosis of the presence or absence of T.equigenitalis. The teachings of Tainturier et al taken together with Friedrich provide a suggestion, motivation and reasonable expectation of obtaining monoclonal antibodies that are specific to T.equigenitalis antigens, the antibodies being diagnostic reagents for the prompt diagnosis of infection. The burden for establishing a prima facie case of obviousness has been met.

33. The rejection of claims 30, 33 and 34 under 35 U.S.C. 103(a) as being unpatentable over Tainturier in view of Friedrich and Harlow further in view of Foster (US Pat. 4,444,879), is traversed on the grounds that Foster's teachings "fails to teach the kits which include Applicant's claimed antibodies or fragments".

34. It is the position that the scope of the claims clearly includes the antibodies described in the instant specfication, but no specific antibodies are recited in the claims. Foster was cited to teach the formulation of kits and the components needed for carrying out an immunoassay, wherein the

kit provides a means for carrying out the immunoassay test in a simple, econonical and rapid basis (see Foster: col. 6, lines 4-6). One of ordinary skill in the art would have been motivated by the reasonable expectation of success of formulating the monoclonal antibodies of Tainturier in view of Friedrich and Harlow into kit for the realized advantages kits provide to the end user which include more stable reagents (see Foster, col. 6, line 11), less training required in their use than those associated with other known methods (see Foster, col. 6, line 12) and safer to use (see Foster, col.6, line 15).

New Claim Limitations/New Grounds of Objection/Rejection

Claim Objections

35. Claims 17-19, 22, 24,26,29, 35, 28, 27, 20, 33,34 and 31 are objected to because of the following informalities: All of the claim recite the term "aqui" which should be --equi--. All of the claims recite the term "Psfluorescens" should be --Pseudomonas fluorescens-- . Claim 17 recites abbreviations that have not been defined at their first appearing in the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

36. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

37. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 30 has been amended to recite non-elected inventions.

38. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

39. Claims 17-19, 22, 24,26,29, 35, 28, 27, 20, 33 ,34 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. All of the claims have been amended to recite the phrase "do not exhibit a crossed reaction with **at least** K pneumoniae, Psfluorescens, St aureus, Str aqui, P haemolytica, P multocida, Ps aeruginosa and Act equuli" but the specification does not provide original descriptive support for the recited range of non-cross reactive monoclonal antibodies, as the antibodies of the instant specification only were reacted with 8 different bacteria, and not the genus of strains now recited . All of the claims recite new matter. This rejection could be obviated by amending the claims to delete the phrase [at least].

Conclusion

40. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

41. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp October 7, 2002

L. F. S.

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